EUROIMMUN Medizinische Labordiagnostika AG

Diagnosing Alzheimer's disease

A new generation of test systems from EUROIMMUN

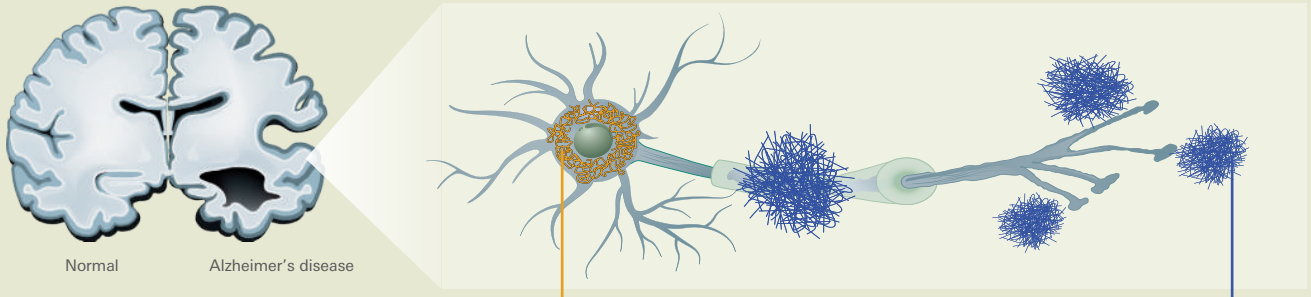
- ELISAs and ChLIAs for the detection of beta-amyloid, total tau and pTau
- RT-PCR for the molecular genetic detection of the APOE genotype
- Efficient performance of antigen tests, e.g. due to standardised protocols
- Convenient automation solutions for all test systems
- Improved diagnostics due to amyloid quotient determination

Alzheimer’s disease

Alzheimer's disease is with 60% to 70% the most common cause of dementia in old age. It is characterised by progressive and irreversible deterioration of cognitive abilities. The disease generally starts with mild symptoms and ends with severe damage of the brain.

Pathology

In the brain of a patient with Alzheimer’s disease, protein deposits form within and outside the nerve cells, which lead to destruction of the nerve cells.

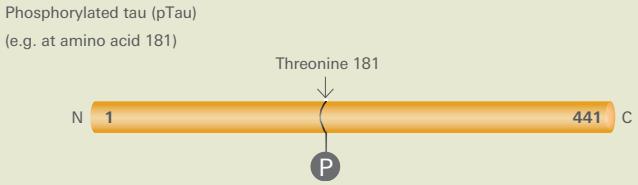


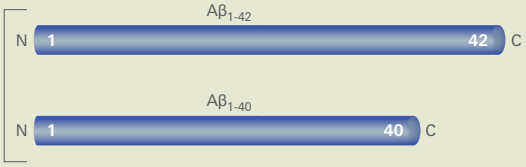
Tau

The tau protein is expressed in neurons in order to stabilise the microtubuli of the cytoskeleton. The erroneous phosphorylisation of this protein leads to the formation of aggregates, which accumulate as so-called neurofibrillary tangles in the nerve cell bodies. Consequently, the axonal transport is disturbed.

Beta-amyloid

The processing of the neuronal, membrane-based amyloid precursor protein (APP) leads to the formation of different isoforms of the peptide beta-amyloid (including $A\beta_{1\text{-}42}$ and $A\beta_{1\text{-}40}$). In Alzheimer’s disease, the breakdown of these peptides is disturbed. The $A\beta_{1\text{-}42}$ isoform aggregates and forms plaques outside of the neurons.





Diagnosis

Suspected diagnosis is based primarily on the identification of **clinical symptoms**. To support the finding, **imaging techniques** are applied. Especially in early and pre-symptomatic stages of Alzheimer’s disease, the clinical diagnosis is complemented by the detection of measurable **biomarkers**. For diagnosis, all available diagnostic information is compiled and then examined and evaluated.

CLINICAL SYMPTOMS

The clinical signs of Alzheimer’s disease may differ a lot. Common symptoms are, amongst other things, memory loss that disrupts daily life, problems understanding visual and spatial relationships, trouble in finding words, withdrawal from social activities and changes in personality, up to depression.

IMAGING TECHNIQUES

If symptoms are present, structural imaging e.g. using MRT or CT should be performed in order to identify typical atrophy patterns and exclude other causes of cognitive impairment. Moreover, PET imaging can help detect and quantify amyloid deposits in the brain.

BIOMARKERS

Beta-amyloid: The CSF of persons who will develop Alzheimer’s disease exhibits significantly decreased concentrations of the Aβ1-42 isoform or a decreased quotient of Aβ1-42 to Aβ1-40 even before the onset of cognitive changes.

Tau: The concentrations of unphosphorylated (total tau) and phosphorylated tau (pTau) in the CSF of patients increase with progressing neurodegeneration and cognitive impairment.

RISK FACTORS

ApoE plays a role in the breakdown of beta-amyloid. Carriers of an APOE-ε4 allele have an increased risk of developing Alzheimer’s disease and side effects (ARIA) under anti-beta-amyloid antibody treatment.

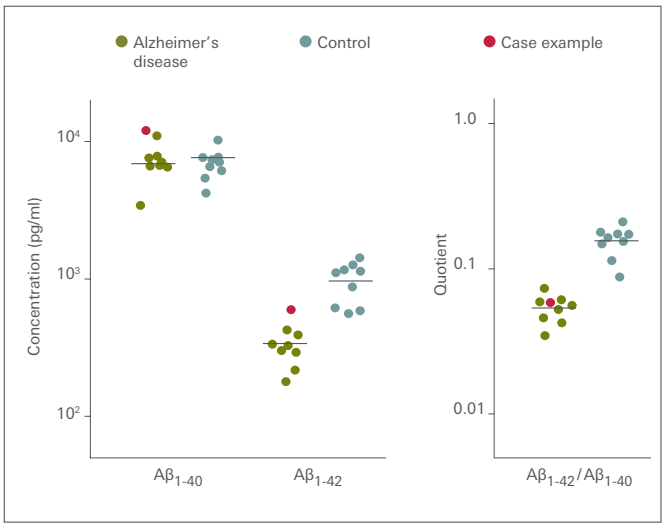
Improved early and differential diagnosis by amyloid quotients

Amyloid concentration and quotient determination

Determination of the $A\beta_{1-42}/A\beta_{1-40}$ quotient can improve the efficiency of early diagnosis. $A\beta_{1-40}$ is a measure of the individual amyloid expression and remains unchanged by Alzheimer's disease. The case study shows the CSF results for a patient with a high basal expression of beta amyloids. If only $A\beta_{1-42}$ is considered, the patient cannot be clearly identified. This can only be done by quotient formation.

Studies have shown that diagnoses based on the $A\beta_{1-42}/A\beta_{1-40}$ quotient correlate better with amyloid-PET results than diagnoses based solely on the $A\beta_{1-42}$ concentration (93% vs. 83% agreement).

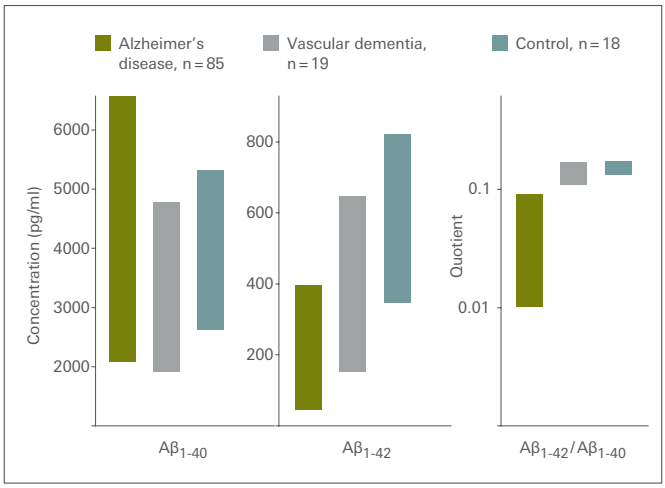
Janelidze S, et al. Ann Clin Transl Neurol 3(3):154-65 (2016).



Differential diagnostics

The figure shows that the determination of the amyloid quotient can also help in the clinically difficult differentiation between Alzheimer's and vascular dementia. The cut-off for the $A\beta_{1-42}/A\beta_{1-40}$ quotient is 0.1 (for EUROIMMUN ELISAs):

- Quotient < 0.1: Abnormal Aβ value, decreased $A\beta_{1-42}$ concentration
- Quotient > 0.1: normal Aβ value



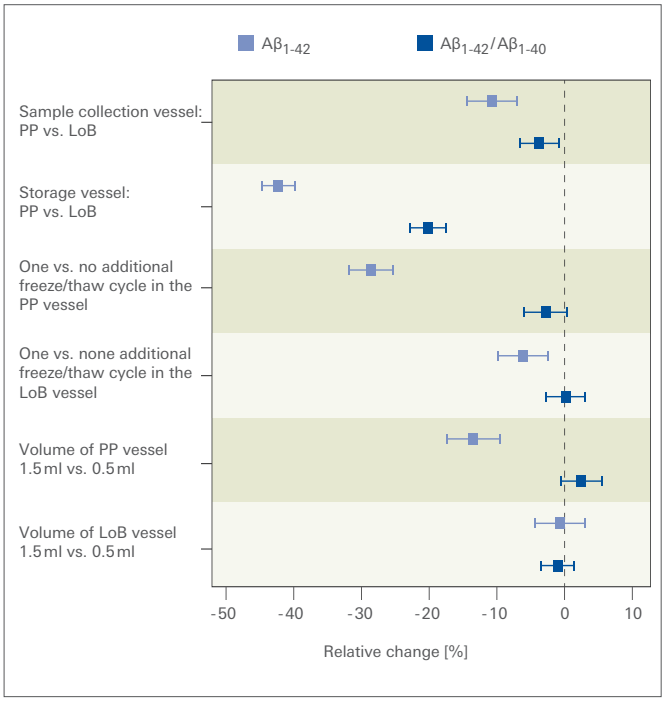
Influence of external factors on $A\beta_{1-42}$

In particular, the determination of the $A\beta_{1-42}$ concentration in CSF is affected in laboratory practice by different external factors. Amongst other things, material and volume of the reaction vessels and the number of freeze/thaw cycles can have a significant influence on the amount of beta-amyloid. The isoforms $A\beta_{1-42}$ and $A\beta_{1-40}$ are subject to these influences (e.g. adsorption by polypropylene vessels) to the same extent. Also due to this reason, the determination of the $A\beta_{1-42}/A\beta_{1-40}$ quotient is the more suitable analysis method, since it is more resistant to changes by external influencing factors. This was shown in a study, e.g. by Vanderstichele et al.: The right figure shows the influence of different parameters on the concentration of $A\beta_{1-42}$ and on the $A\beta_{1-42}/A\beta_{1-40}$ quotient.

Based on this, the Alzheimer's Association and leading researchers published an international guideline for preanalytics in Alzheimer's diagnostics in 2021. It combines existing recommendations in a standardised protocol, with a focus on routine procedures in specialised analysis laboratories.

Hansson O, et al. Alzheimers Dement 17(9):1575-1582 (2021).

EUROIMMUN has recompiled supplementary information in an extensive brochure:
Preanalytics in dementia diagnostics (available upon request).



PP: Polypropylene vessel (Sarstedt); LoB: Low-binding vessel (Eppendorf)
Acc. to Vanderstichele H, et al. J Alzheimers Dis 53(3):1121-32 (2016).

Alzheimer's diagnostics from EUROIMMUN – convenient and precise

EUROIMMUN offers ELISAs and ChLIAs for the detection of beta-amyloid isoforms, total tau and phosphorylated tau (pTau) for comprehensive diagnostics of Alzheimer's disease. The portfolio also includes a microarray and a RT-PCR for the molecular genetic detection of the APOE alleles ε2, ε3 and ε4. The tests meet the high demands of state-of-the-art laboratory routine:

- Parallel performance of beta-amyloid and tau tests enabled e.g. through the use of identical incubation protocols
- Completely automatable processing of all test systems
- Continuous sample loading during the run for the ChLIA systems

More efficiency for your laboratory with our ChLIA systems

- Maximum flexibility in the laboratory routine, providing fast results due to random access.
- Highly precise results owing to the standard calibration curve with 7 to 8 calibrators
- High degree of standardisation due to exclusively completely automated processing
- Complete ChLIA portfolio for the analysis of established CSF biomarkers Aβ(1-40), Aβ(1-42), total tau and pTau(181) from one manufacturer
- Very good correlation of results in comparison with corresponding Lumipulse test systems

IDS-iSYS Multi-Discipline Automated System

Random access solutions

- Convenient benchtop systems
- High throughput of up to 85 samples per hour, first results after only 25 minutes
- Automated identification of patient samples and reagents by barcode recognition for complete traceability
- Time saving in laboratory routine due to permanent on-board reagent storage
- Connection to a laboratory track system possible (IDS-i10)
- Parallel loading of STAT samples possible (IDS-i10)

IDS-i10

Analyte	Sample	Order number			
		ELISA	ChLIA	Microarray	RT-PCR
Beta-amyloid(1-40)	CSF	EQ 6511-9601-L	LQ 6511-10010-L	–	–
Beta-amyloid(1-42)	CSF	EQ 6521-9601-L	LQ 6521-10010-L	–	–
Total-tau	CSF	EQ 6531-9601-L	LQ 6531-10010-L	–	–
pTau(181)	CSF	EQ 6591-9601-L	LQ 6591-10010-L	–	–
APOE (ε2, ε3 and ε4)	Blood	–	–	MN 5710-####	MP 5710-####

ORDER INFORMATION

TOGETHER AT THE PULSE OF NEUROLOGY

neurodiagnostics@euroimmun.de

EUROIMMUN Medizinische Labordiagnostika AG · Seekamp 31 · 23560 Lübeck (Germany) · Phone: +49 451 20 32-0 · www.euroimmun.com

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